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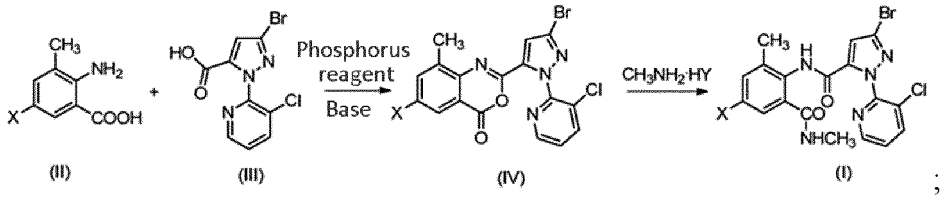
(71) Applicant: **Max (Rudong) Chemicals Co., Ltd.**
Jiangsu 361012 (CN)

(72) Inventors:
- **GUAN, Baochuan**
  Hangzhou
  Zhejiang 310052 (CN)
- **ZHANG, Tianhao**
  Hangzhou
  Zhejiang 310052 (CN)
- **SHENG, Qiuju**
  Hangzhou
  Zhejiang 310052 (CN)
- **CHEN, Bangchi**
  Hangzhou
  Zhejiang 310052 (CN)

(74) Representative: **Haseltine Lake Kempner LLP**
Redcliff Quay
120 Redcliff Street
Bristol BS1 6HU (GB)

(54) METHOD FOR PREPARING N-ACYL ORTHO-AMINOBENZAMIDE

(57) Disclosed herein is a method of preparing N-acyl anthranilamide (I), including: reacting a substituted anthranilic acid (II) with pyrazolecarboxylic acid (III) under the action of a phosphorus reagent and a base to obtain an intermediate benzoxazinone (IV); and subjecting the intermediate benzoxazinone(IV) and a protonic acid salt of methylamine to a ring-opening reaction to obtain N-acyl anthranilamide (I), as shown in the following reaction scheme:



(II) (III) (IV) (I) ;

where X is hydrogen, chloro or cyano group; and HY is hydrohalic acid, sulfuric acid, phosphoric acid or a carboxylic acid. The method has the advantages of simple operation, mild reaction conditions, less waste and high overall yield, and thus is suitable for industrial production.

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Description

TECHNICAL FIELD

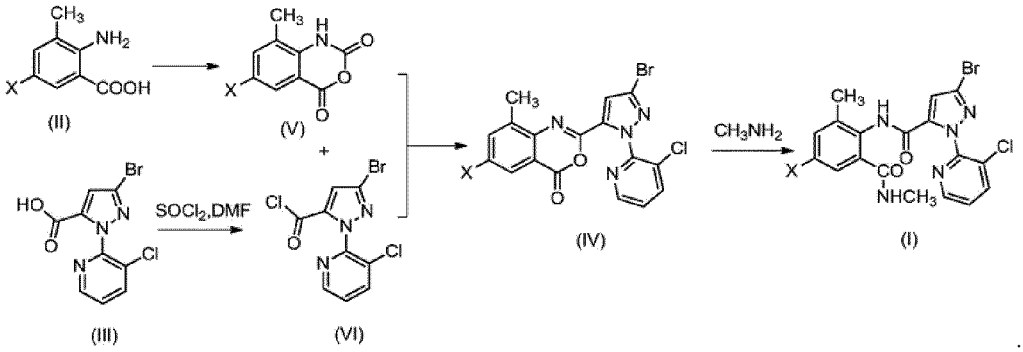
[0001] This application relates to organic synthesis, and more specifically to a method of preparing N-acyl anthranilamide.

BACKGROUND

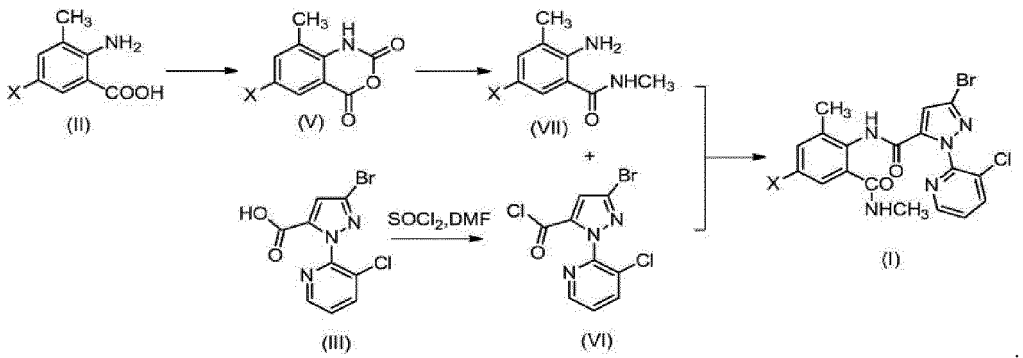
[0002] N-Acyl anthranilamides (I) (as shown hereinafter) are an important class of organic compounds which are widely used in pesticides, medicines and other fields. For example, 3-bromo-N-(2-methyl-4-chloro-6-(carbamoyl)phenyl)-1-(3-chloro-2 -pyridinyl)-1H-pyrazole-5-carboxamide (X is chloro, chlorantraniliprole) and 3-bromo-N-(2-methyl-4-cyano-6-(carbamoyl)phenyl)-1-(3-chloro-2-pyridinyl)-1H -pyrazole-5-carboxamide (X is cyano, cyantraniliprole) developed by DuPont Company are two important N-acyl anthranilamide insecticides, which mainly act on ryanodine receptors of insects and are used to control most chewing pests, especially *Lepidoptera, Coleoptera* and *Diptera,* and thus they are suitable for the pest control for fruit trees, vegetables, grape berries, cotton, sugar cane, rice, lawns and etc.

[0003] Currently, there are mainly three methods for synthesizing N-acyl anthranilamide (I) using a substituted anthranilic acid (II) and pyrazolecarboxylic acid (III) as raw materials.

[0004] In method 1, a substituted anthranilic acid (II) is dehydrated and cyclized under the action of a formyl chlorinating reagent (such as methyl chloroformate and phosgene) to obtain an intermediate isatoic anhydride (V), and pyrazolecarboxylic acid (III) is converted to pyrazolecarboxylic chloride (VI) under the action of thionyl chloride and DMF. Then, the isatoic anhydride (V) and pyrazolecarboxylic chloride (VI) are condensed under the action of an acid binding agent such as pyridine to give an intermediate benzoxazinone (IV). Then the latter undergoes further a ring-opening reaction with methylamine to produce N-acyl anthranilamide (I) (WO2003/015519). The reaction scheme is shown as follows:

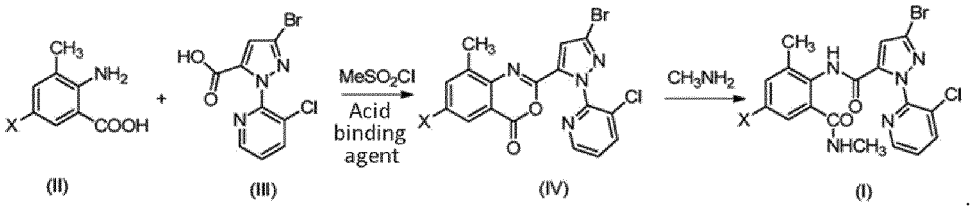


[0005] In method 2, a substituted anthranilic acid (II) is dehydrated and cyclized under the action of a formyl chlorinating reagent (such as methyl chloroformate and phosgene) to obtain an intermediate isatoic anhydride (V). The latter undergoes a ring-opening reaction with methylamine to give anthranilamide (VII). Pyrazolecarboxylic acid (III) is converted to pyrazolecarboxylic chloride (VI) under the action of thionyl chloride and DMF. Then the pyrazolecarboxylic chloride (VI) and the anthranilamide (VII) are condensed under an acid binding agent to produce N-acyl anthranilamide (I) (WO2008/010897). The reaction scheme is shown as follows:



[0006] Methods 1 and 2 both have a relatively long reaction steps, and more over require highly-toxic reagents such as methyl chloroformate and phosgene, resulting in operational inconveniences and unsuitability for industrial production.

[0007] In method 3, a substituted anthranilic acid (II) is reacted with pyrazolecarboxylic acid (III) under the action of methanesulfonyl chloride and an acid binding agent to give an intermediate benzoxazinone (IV), which is then reacted with a solution of methylamine in tetrahydrofuran to obtain N-acyl anthranilamide (I) (WO2003/015519). The reaction scheme is specifically shown as follows:



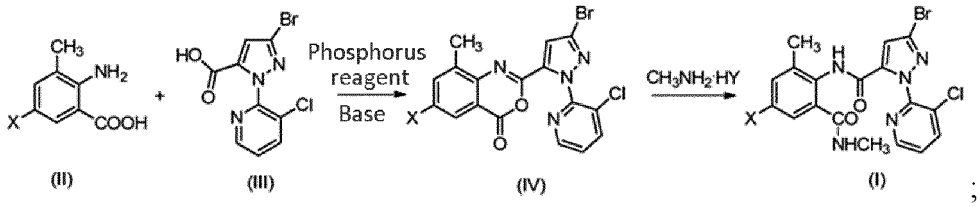
[0008] Although this method involves fewer steps compared to methods 1 and 2, it requires an excessive amount of methanesulfonyl chloride, which leads to the production of a large amount of difficult to treat and highly polluting sulfur-containing organic acid wastewater. In addition, this method involves low yield (the two-step total yield is about 20%), unsuitable for industrial production.

SUMMARY

[0009] This application provides a simpler, more environmentally-friendly and more efficient method of preparing N-acyl anthranilamide (I) to overcome the above drawbacks in the prior art.

[0010] This application provides a method of preparing N-acyl anthranilamide (I), comprising:

step (1) reacting a substituted anthranilic acid (II) with pyrazolecarboxylic acid (III) under the action of a phosphorus reagent and a base to obtain an intermediate benzoxazinone (IV); and
step (2) subjecting the intermediate benzoxazinone (IV) and a protonic acid salt of methylamine to a ring-opening reaction to obtain N-acyl anthranilamide (I), as shown in the following reaction scheme:



;

wherein:

X is hydrogen, chloro or cyano group; and
HY is hydrohalic acid, sulfuric acid, phosphoric acid or a carboxylic acid, preferably hydrochloric acid or sulfuric acid.

[0011] The phosphorus reagent is a phosphorus-containing compound, such as phosphorus oxychloride, phosphorus oxybromide, phosphorus trichloride, phosphorus tribromide, phosphorus pentachloride or phosphorus pentabromide, preferably phosphorus oxychloride or phosphorus oxybromide.

[0012] The base used in step (1) is an organic base or an inorganic base, preferably an organic base, and more preferably a tertiary amine base such as pyridine, 3-methylpyridine, N,N-dimethylaminopyridine and triethylamine.

[0013] In step (1), a molar ratio of the compound (II) to the compound (III) is 1:0.5-1.5; a molar ratio of the compound (II) to the phosphorus reagent is 1:1-2; and a molar ratio of the compound (II) to the base is 1:2-5.

[0014] In step (2), the ring opening reaction may be performed in the presence of an appropriate amount of a base, where the base is an organic base or an inorganic base, preferably an organic base such as triethylamine, pyridine and 3-methylpyridine, and a molar ratio of the compound (IV) to the base is 1:1-3.

[0015] A molar ratio of the compound (IV) to the protonic acid salt of methylamine is 1:1-3.

[0016] A solvent used herein is selected from N,N-dimethylformamide, acetone or acetonitrile, preferably acetonitrile.

[0017] Compared to the prior art, the method provided herein of preparing N-acyl anthranilamide has the following

advantages.

(1) This method has simple process and mild reaction conditions.
(2) This method avoids the use of toxic substance such as methyl chloroformate or phosgene and is easy to operate.
(3) This method is free of production of sulfur-containing organic acid wastewater caused by organic reagent, such as methanesulfonyl chloride, and has less pollution.
(4) This method is high yielding, suitable for industrial production.

DETAILED DESCRIPTION OF EMBODIMENTS

[0018] Features of this application will be further illustrated below with reference to the embodiments, but these embodiments are not intended to limit this application.

Example 1 Preparation of **3-bromo-N-(2-methyl-4-chloro-6-(carbamoyl) phenyl)-1-(3-chloro-2-pyridinyl)-1H-pyrazole-5-carboxamide (chlorantraniliprole)**

Step (1)

[0019] 3.02 g of 3-bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazole-5-carboxylic acid, 1.95 g of 3-methylpyridine and 15 mL of acetonitrile were added to a 100 mL three-necked flask, to which 5.73 g of $POBr_3$ was dropwise added at -5°C. The reaction mixture was stirred for 0.5 h with the temperature kept, and then 1.86 g of 2-amino-3-methyl-5-chlorobenzoic acid was added. The reaction mixture was reacted at room temperature for 1 h. After the reaction was complete, the reaction mixture was added with 20 mL of water, stirred for 0.5 h and filtered. The filter cake was washed with a mixture of acetonitrile and water in a ratio of 3:2 and dried to give 4.16 g of 2-[3-bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazol-5-yl]-6-chloro-8-methyl-4H-3,1-benzoxazine- 4-one, and the yield was 92%.

Step (2)

[0020] 4.16 g of 2-[3-bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazol-5-yl]-6-chloro-8-methyl-4H-3,1-benzoxazine-4-one obtained in step (1) was dissolved in 20 mL of acetonitrile, to which 0.92 g of methylamine hydrochloride was added. The reaction mixture was stirred at room temperature for 4 h, desolventized under vacuum, washed with water and dried to give 3.56 g of chlorantraniliprole, and the yield was 80%.

Example 2 Preparation of **3-bromo-N-(2-methyl-4-chloro-6-(carbamoyl) phenyl)-1-(3-chloro-2-pyridinyl)-1H-pyrazole-5-carboxamide (chlorantraniliprole)**

Step (1)

[0021] 3.02 g of 3-bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazole-5-carboxylic acid, 1.95 g of 3-methylpyridine and 15 mL of acetonitrile were added to a 100 mL three-necked flask, to which 5.73 g of $POBr_3$ was dropwise added at -5°C. The reaction mixture was stirred for 0.5 h with the temperature kept, and then 1.86 g of 2-amino-3-methyl-5-chlorobenzoic acid was added. The reaction mixture was reacted at room temperature for 1 h. After the reaction was complete, the reaction mixture was added with 20 mL of water, stirred for 0.5 h and filtered. The filter cake was washed with a mixture of acetonitrile and water in a ratio of 3:2 and dried to give 4.16 g of 2-[3-bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazol-5-yl]-6-chloro-8-methyl-4H-3,1-ben zoxazine- 4-one, and the yield was 92%.

Step (2)

[0022] 4.16 g of 2-[3-bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazol-5-yl]-6-chloro-8-methyl-4H-3,1-benzoxazine-4-one obtained in step (1) was dissolved in 20 mL of acetonitrile, to which 1.11 g of triethylamine and 0.92 g of methylamine hydrochloride were added. The reaction mixture was stirred at room temperature for 2 h, desolventized under vacuum, washed with water and dried to give 4.18 g of chlorantraniliprole, and the yield was 94%.

Example 3 Preparation of **3-bromo-N-(2-methyl-4-chloro-6-(carbamoyl) phenyl)-1-(3-chloro-2-pyridinyl)-1H-pyrazole-5-carboxamide (chlorantraniliprole)**

Step (1)

[0023] 4.53 g of 3-bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazole-5-carboxylic acid, 1.58 g of pyridine and 15 mL of acetonitrile were added to a 100 mL three-necked flask, to which 3.07 g of $POCl_3$ was dropwise added at -5°C. The reaction mixture was stirred for 0.5 h with the temperature kept, and then 1.86 g of 2-amino -3-methyl-5-chlorobenzoic acid was added. The reaction mixture was reacted at room temperature for 0.5 h. After the reaction was complete, the reaction mixture was added with 20 mL of water, stirred for 0.5 h and filtered. The filter cake was washed with a mixture of acetonitrile and water in a ratio of 3:2, and dried to give 4.07 g of 2-[3-bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazol-5-yl]-6-chloro-8-methyl-4H-3,1-ben zoxazine-4-one, and the yield was 90%.

Step (2)

[0024] 4.07 g of 2-[3-bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazol-5-yl]-6-chloro-8-methyl-4H-3,1-benzoxazine-4-one obtained in step (1) was dissolved in 20 mL of acetonitrile, to which 2.73 g of triethylamine, pyridine and 1.82 g of methylamine hydrochloride were added. The reaction mixture was stirred at room temperature for 2 h, desolventized under vacuum, washed with water and dried to give 4.17 g of chlorantraniliprole, and the yield was 96%.

Example 4 Preparation of 3-bromo-N-(2-methyl-4-chloro-6-(carbamoyl) phenyl)-1-(3-chloro-2-pyridinyl)-1H-pyrazole-5-carboxamide (chlorantraniliprole)

Step (1)

[0025] 3.02 g of 3-bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazole-5-carboxylic acid, 4.87 g of 3-methylpyridine and 30 mL of acetonitrile were added to a 100 mL three-necked flask, to which 5.73 g of $POBr_3$ was dropwise added at -5°C. The reaction mixture was stirred for 0.5 h with the temperature kept, and then 1.86 g of 2-amino-3-methyl-5-chlorobenzoic acid was added. The reaction mixture was reacted at room temperature for 1.5 h. After the reaction was complete, the reaction mixture was added with 20 mL of water, stirred for 0.5 h and filtered. The filter cake was washed with a mixture of acetonitrile and water in a ratio of 3:2, and dried to give 4.2 g of 2-[3-bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazol-5-yl]--chloro-8-methyl-4H -3,1-benzoxazine-4-one, and the yield was 93%.

Step (2)

[0026] 4.2 g of 2-[3-bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazol-5-yl]-6-chloro-8-methyl-4H-3,1-benzoxazine-4-one obtained in step (1) was dissolved in 20 mL of acetonitrile, to which 1.23g of 4-dimethylaminopyridine and 2.18 g of methylamine sulfate were added. The reaction mixture was stirred at room temperature for 2.5 h, desolventized under vacuum, washed with water and dried to give 4.27 g of chlorantraniliprole, and the yield was 95%.

Example 5 Preparation of 3-bromo-N-(2-methyl-4-chloro-6-(carbamoyl) phenyl)-1-(3-chloro-2-pyridinyl)-1H-pyrazole-5-carboxamide (chlorantraniliprole)

Step (1)

[0027] 3.02 g of 3-bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazole-5-carboxylic acid, 1.95 g of 3-methylpyridine and 15 mL of acetonitrile were added to a 100 mL three-necked flask, to which 5.73 g of $POBr_3$ was dropwise added at -5°C. The reaction mixture was stirred for 0.5 h with the temperature kept, and then 1.86 g of 2-amino-3-methyl-5-chlorobenzoic acid was added. The reaction mixture was reacted at room temperature for 1 h. After the reaction was complete, the reaction mixture was added with 20 mL of water, stirred for 0.5 h and filtered. The filter cake was washed with a mixture of acetonitrile and water in a ratio of 3:2 and dried to give 4.16 g of 2-[3-bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazol-5-yl]-6-chloro-8-methyl-4H-3,1-benzoxazine- 4-one, and the yield was 92%.

Step (2)

[0028] 4.16 g of 2-[3-bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazol-5-yl]-6-chloro-8-methyl-4H-3,1-benzoxazine-4-one obtained in step (1) was dissolved in 20 mL of acetonitrile, to which 0.79 g of pyridine and 0.92 g of methylamine hydrochloride were added. The reaction mixture was stirred at room temperature for 1.5 h, desolventized under vacuum,

washed with water and dried to give 4 g of chlorantraniliprole, and the yield was 90%.

Example 6 Preparation of 3-bromo-N-(2-methyl-4-cyano-6-(carbamoyl) phenyl)-1-(3-chloro-2-pyridinyl)-1H-pyrazole-5-carboxamide (cyantraniliprole)

Step (1)

[0029] 3.02 g of 3-bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazole-5-carboxylic acid, 1.95 g of 3-methylpyridine and 15 mL of acetonitrile were added to a 100 mL three-necked flask, to which 3.23 g of $POCl_3$ was dropwise added at -5°C. The reaction mixture was stirred for 0.5 h with the temperature kept, and 1.94 g of 2-amino-3-methyl-5-cyanobenzoic acid was added. The reaction mixture was reacted at room temperature for 2 h. After the reaction was complete, the reaction mixture was added with 20 mL of water, stirred for 0.5 h and filtered. The filter cake was washed with a mixture of acetonitrile and water in a ratio of 3:2 and dried to give 3.81 g of 2-[3-bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazol-5-yl]-6-cyano-8-methyl-4H-3,1-benzoxazine-4-one, and the yield was 86%.
^{1}H NMR (500MHz, DMSO): δ8.63 (dd,1H), 8.40-8.33(m,2H), 8.10(s,1H), 7.77(dd,1H), 7.60(s,1H), 1.73(s,3H).

Step (2)

[0030] 3.81 g of 2-[3-bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazol-5-yl]-6-cyano-8 -methyl-4H-3,1-benzoxazine-4-one obtained in step (1) was dissolved in 20 mL of acetonitrile, to which 1.11 g of triethylamine and 2.18 g of methylamine sulfate were added. The reaction mixture was stirred at room temperature for 2.5 h, desolventized under vacuum, washed with water and dried to give 3.87 g of cyantraniliprole, and the yield was 95%.

Example 7 Preparation of 3-bromo-N-(2-methyl-4-cyano-6-(carbamoyl) phenyl)-1-(3-chloro-2-pyridinyl)-1H-pyrazole-5-carboxamide (cyantraniliprole)

Step (1)

[0031] 3.02 g of 3-bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazole-5-carboxylic acid, 1.95 g of 3-methylpyridine and 15 mL of acetonitrile were added to a 100 mL three-necked flask to which 1.62 g of $POCl_3$ was dropwise added at -5°C. The reaction mixture was stirred for 0.5 h with the temperature kept, and 3.88 g of 2-amino-3-methyl-5-cyanobenzoic acid was added. The reaction mixture was reacted at room temperature for 1.5 h. After the reaction was complete, the reaction mixture was added with 20 mL of water, stirred for 0.5 h and filtered. The filter cake was washed with a mixture of acetonitrile and water in a ratio of 3:2 and dried to give 4.17 g of 2-[3-bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazol-5-yl]-6-cyano-8-methyl-4H-3,1-ben zoxazine-4-one, and the yield was 88%.

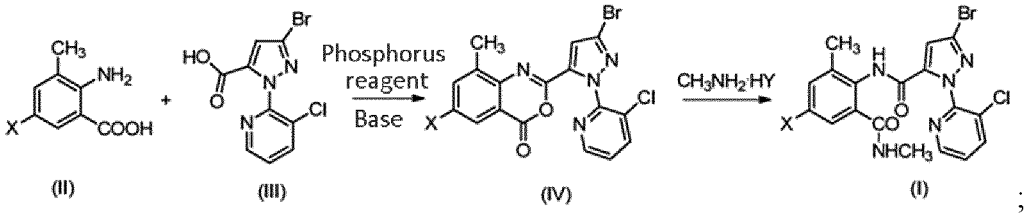
Step (2)

[0032] 4.17 g of 2-[3-bromo-1-(3-chloro-2-pyridinyl)-1H-pyrazol-5-yl]-6-cyano-8 -methyl-4H-3,1-benzoxazine-4-one obtained in step (1) was dissolved in 20 mL of acetonitrile, to which 1.78 g of triethylamine pyridine and 2.82 g of methylamine sulfate were added. The reaction mixture was stirred at room temperature for 2.5 h, desolventized under vacuum, washed with water and dried to give 4.08 g of cyantraniliprole, and the yield was 98%.

Claims

1. A method of preparing N-acyl anthranilamide (I), comprising:

step (1) reacting a substituted anthranilic acid (II) with pyrazolecarboxylic acid (III) under the action of a phosphorus reagent and a base to obtain an intermediate benzoxazinone (IV); and
step (2) subjecting the intermediate benzoxazinone (IV) and a protonic acid salt of methylamine to a ring-opening reaction to obtain N-acyl anthranilamide (I), as shown in the following reaction scheme:



;

wherein:

X is hydrogen, chloro or cyano group; and
HY is hydrohalic acid, sulfuric acid, phosphoric acid or a carboxylic acid.

2. The method according to claim 1, **characterized in that** the phosphorus reagent is phosphorus oxychloride, phosphorus oxybromide, phosphorus trichloride, phosphorus tribromide, phosphorus pentachloride or phosphorus pentabromide.

3. The method according to claim 2, **characterized in that** the phosphorus reagent is phosphorus oxychloride or phosphorus oxybromide.

4. The method according to claim 1, **characterized in that** in step (1), the base is an organic base.

5. The method according to claim 4, **characterized in that** the organic base is pyridine, 3-methylpyridine, N,N-dimethylaminopyridine or triethylamine.

6. The method according to claim 1, **characterized in that** HY is hydrochloric acid or sulfuric acid.

7. The method according to claim 1, **characterized in that** in step (1), a molar ratio of the compound (II) to the compound (III) is 1:0.5-1.5; a molar ratio of the compound (II) to the phosphorus reagent is 1:1-2; and a molar ratio of the compound (II) to the base is 1:2-5.

8. The method according to claim 1, **characterized in that** the step (2) is carried out in the presence of a base.

9. The method according to claim 8, **characterized in that** the base is triethylamine, pyridine or 3-methylpyridine.

10. The method according to claim 1, **characterized in that** in step (2), a molar ratio of the compound (IV) to the protonic acid salt of methylamine is 1:1-3; and a molar ratio of the compound (IV) to the base is 1:1-3.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CN2018/084008

A. CLASSIFICATION OF SUBJECT MATTER

C07D 401/04 (2006.01) i

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CNKI, CNPAT, VEN, CA, CASREACT: 酰基, 邻氨基苯甲酰胺, 农药, 杀虫剂, 苯并噁嗪酮, 吡唑, acyl, aminobenzamide, pesticide, insecticide, benzoxazin+, pyrazol+

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
PX	CN 107089970 A (MAX (RUDONG) CHEMICALS CO., LTD.), 25 August 2017 (25.08.2017), claims 1-10	1-10
X	CN 104003976 A (ZHAOQING ZHENGE BIOTECHNOLOGY CO., LTD.), 27 August 2014 (27.08.2014), embodiment 4	1-10
A	CN 1541063 A (DU PONT), 27 October 2004 (27.10.2004), entire document	1-10
A	CN 103601718 A (JIANGXI TIANREN ECOLOGY CO., LTD.), 26 February 2014 (26.02.2014), entire document	1-10
A	CN 100425607 C (DU PONT), 15 October 2008 (15.10.2008), entire document	1-10

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
23 June 2018	28 June 2018
Name and mailing address of the ISA State Intellectual Property Office of the P. R. China No. 6, Xitucheng Road, Jimenqiao Haidian District, Beijing 100088, China Facsimile No. (86-10) 62019451	Authorized officer WANG, Dawei Telephone No. (86-10) 62086318

Form PCT/ISA/210 (second sheet) (January 2015)

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/CN2018/084008

Patent Documents referred in the Report	Publication Date	Patent Family	Publication Date
CN 107089970 A	25 August 2017	None	
CN 104003976 A	27 August 2014	EP 3141545 A1	15 March 2017
		WO 2015169096 A1	12 November 2015
		US 9301529 B2	05 April 2016
		US 2015322037 A1	12 November 2015
		CN 104003976 B	16 March 2016
		EP 3141545 A4	29 November 2017
CN 1541063 A	27 October 2004	PL 208858 B1	30 June 2011
		PL 368746 A1	04 April 2005
		IN 213177 B	25 January 2008
		US 7696233 B2	13 April 2010
		BR 0212187 A	05 October 2004
		AU 2002355951 C1	16 July 2009
		JP 3689817 B2	31 August 2005
		TW I325302 B	01 June 2010
		TW 200930296 A	16 July 2009
		KR 100847202 B1	17 July 2008
		US 8697734 B2	15 April 2014
		US 2013028879 A1	31 January 2013
		MX 274785 B	26 March 2010
		US 2008275061 A1	06 November 2008
		CA 2454302 C	20 September 2011
		IN 13MU2004 A	09 March 2007
		EP 1416796 B1	27 March 2013
		RU 2004107513 A	10 October 2005
		WO 03015518 A1	27 February 2003
		TW I312274 B	21 July 2009
		ZA 200400034 B	26 October 2005
		IN 438 MU 2005 A	02 December 2005
		US 2010160307 A1	24 June 2010
		CA 2454302 A1	27 February 2003
		AU 2002355951 B2	06 December 2007
		IL 222782 D0	31 December 2012
		NZ 530442 A	28 July 2006
		MX PA04001322 A	20 May 2004
		KR 20040030069 A	08 April 2004
		PH 12004500205 B1	04 December 2009
		BR 0212187 B1	28 May 2013
		AR 038176 A1	05 January 2005
		RU 2262231 C1	20 October 2005
		CN 100425607 C	15 October 2008
		US 2005075372 A1	07 April 2005
		EP 1416796 A1	12 May 2004
		US 2014140973 A1	22 May 2014
		HU 0401043 A2	28 September 2004
		MY 142967 A	31 January 2011
		CO 5550396 A2	31 August 2005
		US 9113630 B2	25 August 2015
		JP 2004538327 A	24 December 2004
		HU 0401043 A3	28 November 2005

Form PCT/ISA/210 (patent family annex) (January 2015)

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/CN2018/084008

Patent Documents referred in the Report	Publication Date	Patent Family	Publication Date
		IL 159513 D0	01 June 2004
CN 103601718 A	26 February 2014	None	
CN 100425607 C	15 October 2008	PL 208858 B1	30 June 2011
		PL 368746 A1	04 April 2005
		IN 213177 B	25 January 2008
		US 7696233 B2	13 April 2010
		BR 0212187 A	05 October 2004
		AU 2002355951 C1	16 July 2009
		JP 3689817 B2	31 August 2005
		TW I325302 B	01 June 2010
		TW 200930296 A	16 July 2009
		KR 100847202 B1	17 July 2008
		US 8697734 B2	15 April 2014
		US 2013028879 A1	31 January 2013
		MX 274785 B	26 March 2010
		US 2008275061 A1	06 November 2008
		CA 2454302 C	20 September 2011
		CN 1541063 A	27 October 2004
		IN 13MU2004 A	09 March 2007
		EP 1416796 B1	27 March 2013
		RU 2004107513 A	10 October 2005
		WO 03015518 A1	27 February 2003
		TW 1312274 B	21 July 2009
		ZA 200400034 B	26 October 2005
		IN 438MU2005 A	02 December 2005
		US 2010160307 A1	24 June 2010
		CA 2454302 A1	27 February 2003
		AU 2002355951 B2	06 December 2007
		IL 222782 D0	31 December 2012
		NZ 530442 A	28 July 2006
		MX PA04001322 A	20 May 2004
		KR 20040030069 A	08 April 2004
		PH 12004500205 B1	04 December 2009
		BR 0212187 B1	28 May 2013
		AR 038176 A1	05 January 2005
		RU 2262231 C1	20 October 2005
		US 2005075372 A1	07 April 2005
		EP 1416796 A1	12 May 2004
		US 2014140973 A1	22 May 2014
		HU 0401043 A2	28 September 2004
		MY 142967 A	31 January 2011
		CO 5550396 A2	31 August 2005
		US 9113630 B2	25 August 2015
		JP 2004538327 A	24 December 2004
		HU 0401043 A3	28 November 2005
		IL 159513 D0	01 June 2004

Form PCT/ISA/210 (patent family annex) (January 2015)

REFERENCES CITED IN THE DESCRIPTION

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Patent documents cited in the description

- WO 2003015519 A **[0004] [0007]**
- WO 2008010897 A **[0005]**